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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,577	07/22/2003	Raymond Pratt	109536.183	6543

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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/623,577	PRATT, RAYMOND	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2 sheets*. 3/23/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Informalities

Claims 36-55 are currently pending and are the subject of this Office Action. Applicant cancelled Claims 1-35 in amendment filed March 23, 2006.

Priority

Applicant removed all claims of priority to prior filed applications in amendment filed March 23, 2006. As such, the earliest effective U.S. filing date is June 22, 2003.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36-40, 42-46, and 48-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ukai *et al.* (U.S. Patent No. 6,576,677; Issued June 10, 2003).

Ukai *et al.* disclose liquid dosage formulations of donepezil hydrochloride comprising polyvinylpyrrolidone, 70% sorbitol, a pH-adjusting agent, preservatives, solvents, antioxidants, and flavoring agents (see especially Columns 6-8). It is further disclosed that the pH of the liquid formulations is usually 3 to 7 (Col. 3, Lines 8-9) and can be adjusted by addition of varying amounts of citric acid.

The reference specifically discloses orally available liquid dosage formulations comprising: (i) 5 mg donepezil HCl (0.1% by weight); (ii) 4.8% by weight povidone K30 (polyvinylpyrrolidone with average M.W. of 40,000); (iii) 34% by weight 70% sorbitol; (iv) 0.2% by weight citric acid; (v) 0.1% by weight sodium benzoate; (vi) 0.02% by weight sodium bisulfite; and (vii) 0.3% by weight flavoring agent (Col. 6, Table 4). The formulation disclosed in Table 4 does not contain a solvent (*e.g.* propylene glycol). However, an alternate formulation disclosed in the reference comprises: (i) 0.1 % by weight donepezil HCl; (ii) 5.7 % by weight povidone K30; (iii) 41% by weight 70% sorbitol; (iv) 0.2% by weight citric acid; (v) 0.1% by weight methylparaben; (vi) 6.9% by weight propylene glycol; and (vii) 0.3% by weight flavoring agent (Col. 8, Example 8). The formulation disclosed in Example 8 does not contain an antioxidant. The formulations disclosed in the reference differ from the instantly claimed formulations in the amount of polyvinylpyrrolidone present in the compositions.

However, Ukai *et al.* also disclose a formulation of donepezil (5 mg), polyvinylpyrrolidone (100 mg) in a total of 5 g solution (2% polyvinylpyrrolidone) (Column 4, Test 2). It is disclosed that the formulations reduce the unpleasant taste generally associated with donepezil liquid compositions (Column 4, Table 1 and Column 5) and when an antioxidant is present in the composition (sodium bisulfite), the formulations are stable for extended periods at elevated temperatures (Column 6, Lines 26-30).

In the absence of a showing of unexpected results, the present formulations would have been *prima facie* obvious given the disclosure of Ukai *et al.* Formulations

comprising the instantly claimed components in amounts encompassed by the present claims are specifically disclosed in the reference. The lower amount of polyvinylpyrrolidone (0.1 to 3%) in the instant claims compared to the 4.8 to 5.7% in the reference formulations would have been obvious given the formulation disclosed in Test 2 (Column 4, Lines 54-60) wherein only 2% polyvinylpyrrolidone and 0.1% donepezil were included in the composition. It is clear from the results in Table 2 that lower amounts of polyvinylpyrrolidone (*e.g.* 2%) demonstrated less numbing and bitter taste than higher amounts of polyvinylpyrrolidone (*e.g.* 10% and 14%). Thus, given these results and disclosure of formulations containing 2%, 4.8%, and 5.7% polyvinylpyrrolidone, in the absence of a showing of unexpected results no unobviousness is seen in the instantly claimed ranges of 0.5 to 2% and 0.1 to 3% polyvinylpyrrolidone. Further, Ukai *et al.* disclose that the larger the molecular weight of polyvinylpyrrolidone, the less the amount of it needs to be added, while the smaller the molecular weight, the more polyvinylpyrrolidone needs to be added (Column 2, Lines 60-62). "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

The skilled artisan would be motivated to modify the formulation of Example 8 in the reference to include an antioxidant given the results of Test 4 (Column 6, Lines 26-30) wherein a formulation containing sodium bisulfite ("Test Sample", Table 4) demonstrated better stability than a formulation wherein the antioxidant was omitted.

Other antioxidants (*e.g.* sodium sulfite, ascorbic acid) are disclosed as being usable in the disclosed formulations (Column 3, Lines 40-45).

Thus, the instantly claimed liquid formulations of donepezil would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 41, 47, and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ukai *et al.* as applied to claims 36-40, 42-46, and 48-54 above, and further in view of Sugimoto *et al.* (U.S. Patent No. 4,895,841; Issued January 3, 1990).

Sugimoto *et al.* disclose that donepezil, its hydrochloride salt, and stereoisomers (see especially Column 34, Example 4 and Column 12, Lines 30-48) are capable of inhibiting acetylcholinesterase and are thus effective for the treatment of various kinds of dementia and cerebrovascular diseases (Column 29, Lines 52-65). The patentees further disclose effective dosages of from generally 0.1 to 300 mg and specifically 1 to 100 mg per day (Column 30, Line 25). The compounds may be orally administered (Column 30, Lines 10-11) and presented in a variety of dosage forms, such as injections, suppositories, sublingual tablets, tablets, and capsules (Col. 30, Lines 27-31).

In the absence of a showing of unexpected results commensurate in scope with the claims, it would have been obvious to formulate liquid compositions comprising the enantiomers of donepezil in the formulations disclosed in Ukai *et al.* The motivation to do is found in Sugimoto who disclose that donepezil, its hydrochloride salt, and

stereoisomers are capable of inhibiting acetylcholinesterase and are thus effective for the treatment of various kinds of dementia and cerebrovascular diseases.

Thus, the instant claims, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Examiner
Art Unit 1614

June 1, 2006

Ardin H. Marschel 6/11/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER